Freedom to Fund

Philanthropists are exerting an unmistakable influence on the research agenda, drawing attention to long-ignored research areas, promoting collaborations, and giving scientists the freedom to explore serendipitous ideas. Unbridled by politics or bureaucracy, philanthropic organizations can fund the riskier projects that could yield the biggest payoffs.

With RO1 individual investigator grants from the National Institutes of Health (NIH) becoming more difficult to obtain, researchers are seeking fresh sources of funding from philanthropic organizations. "We're starting to bleed here at the University of Washington. Postdocs and technicians are being laid off," says George Martin, who studies aging. His institution is not alone. "It's happening all over the country. High-impact research institutes thrive on soft money and they're hit the hardest," says Martin, who receives funding from the Alzheimer's Association and the M.J. Murdock Charitable Fund. "I don't see the possibility of any substantial increases in [NIH funding] so the money will have to come from private sources."

Funding Risky Research, Forging New Collaborations

Traditional NIH grants usually fund rigidly defined projects, whereas funds from philanthropic organizations can give scientists the freedom to undertake risky research and to forge ambitious collaborations. For example, the ability to join talented people together to tackle large-scale research projects is a defining strength of the Broad Institute in Cambridge, Massachusetts. The Institute's philanthropic backers, Eli and Edythe L. Broad, initially provided $100 million, to be spent at the rate of $10 million per year for 10 years, and then soon doubled this gift to $200 million. The Institute's 114 faculty consist of 6 core members, who are located at the Broad Institute, and 108 associate members whose primary labs are located at other world-class biomedical facilities in the area. These facilities are often referred to as vertical silos, says Eric Lander, founding director of the Broad Institute and a professor at MIT, Harvard Medical School, and the Whitehead Institute for Biomedical Research. "There are all the departments at MIT, all the departments at Harvard, the medical school, the school of public health, the teaching hospital, etcetera, and the Broad is a horizontal connector between all of those," says Lander. Although the Broad funds constitute a minority of the Institute's budget, "The Broad funds are what make the Broad possible," says Lander. He says that while the NIH system forms the backbone of biomedical research, it's necessarily conservative and, "We need other sources of funds that are not conservative." Lander calls the Broad funding "academic venture funds to try experiments." "We're doing experiments on how to do science," says Lander. "Broad is an experiment that says we should take risks on building datasets that might fail." As an example, Lander points to the connectivity map spearheaded by Todd Golub, the director of the Broad Institute's Cancer program. The map is a database of the genetic signatures of various drugs, "You take drugs, put them on cell lines, look at their whole expression pattern and make a database. It turns out that by doing that you can take up all sorts of connections between drugs that you never knew—that drug X might be useful for disease Y because of its expression pattern," says Lander. "If you went to a study section and told them you want to develop this kind of database, they'd say, what a fishing expedition. This is the sort of project we use Broad funds for." The Institute also fosters creativity with its Scientific Planning and Allocation of Resources Committee (SPARC). SPARC proposals have been funded for small amounts like $40,000 or for $1 million or more, says Lander. "They can move rapidly because the death knell of creativity is to tell a young scientist that she should write a grant proposal for her great idea and three years later get the money to try it," says Lander.

The Broad Institute isn't the only philanthropic organization to encourage young scientists to aim high. The John D. and Catherine T. MacArthur Foundation, one of the largest private philanthropic foundations in the US, fosters progress by identifying the very brightest, most creative minds in all disciplines and providing them with resources to help them live up to their potential. In September last year, Kevin Eggan, an embryonic stem cell researcher at the Harvard Stem Cell Institute, received a phone call informing him that he'd been awarded one of the MacArthur Foundation's so-called "genius" grants—$500,000 over 5 years to spend in any way he sees fit. MacArthur fellows are nominated and selected anonymously and are chosen for their potential rather than for their prior successes. "[The fellowship] provides flexibility to do things that I wouldn't otherwise be able to do," says Eggan. "The MacArthur foundation is a very forward thinking, thoughtful organization; to give us this award means they've thought deeply about stem cell research," he says.

Embryonic stem cell research and other controversial or politically sensitive research areas are heavily dependent on philanthropic funding for their survival. Because US federal funds cannot be used to support embryonic stem cell research, private philanthropists are stepping in to fill the gap. The Charles C. and June S. Gates Family Fund trustees recently committed $6 million to the University of Colorado at Denver and the Health Sciences Center to establish the Charles C. Gates Regenerative Medicine and Stem Cell Biology Program. Meanwhile, in California, the Dolby Foundation (founded by

sound pioneer Ray Dolby of Dolby Laboratories) donated $5 million to ensure that stem cell research at the fledgling California Institute for Regenerative Medicine (CIRM) could move forward, after public funds were blocked by a court challenge.

Patients Boost Funds for Biomedical Research

Cancer survivors Jim and Virginia Stowers, founders of American Century Investments, created the Stowers Institute for Medical Research in 2000 with a very focused mission to support basic research on cell proliferation, differentiation, and cell death during early development. The Institute, housed on a 10-acre campus in Kansas City, Missouri, offers its scientists state of the art technical support with access to advanced imaging systems, transgenic animal and microarray facilities, and other costly infrastructure. "We allow our researchers to rely on a very strong base of support to undertake risky experiments that would never attract funding from the NIH or from any other rather risk averse funding agency," says reproductive endocrinologist William Neaves, President and CEO of the Stowers Institute. "We can tell people that if you come here, we will make sure you will have a high level of collaborative support from one of the best proteomics facilities in the world and access to a tech center with state of the art mass spectrometer facilities," says Neaves. "We offer those who join us here a collaborative environment that offers them an opportunity to do more important work than any of them can do alone."

Philip Kantoff, chief clinical research officer at the Dana Farber Cancer Institute in Boston, has received numerous donations from grateful patients as well as from private groups like the Prostate Cancer Foundation (founded by prostate cancer survivor and billionaire Michael Milken). Kantoff says he's had some patients write him a check and say "here's some money to spend on research," but he's also had philanthropists approach and say, "here's my foundation, let's see if we can get you a grant." Some patients send in small donations, but in one instance he received $5 million for his research. This charitable money gives Kantoff the freedom to support innovative cancer research in his lab and others at the Dana Farber. NIH grants pay for the specific project proposed in the grant, but nothing more—there's no extra money in the grant to pay for stepping out of the box and that's where the exciting work happens, says Kantoff.

Often an exciting result leads a researcher beyond the realm of a narrowly defined project, and it might take months or years for a scientist to apply for and receive the additional funding necessary to pursue the promising lead. The Michael J. Fox Foundation, which funds research on Parkinson's disease, is hoping to speed up this process with its new Rapid Response Innovation Awards. The grants of up to $75,000 are meant to allow researchers to quickly access the funds they need to follow through on new ideas. "It's a three-page grant application," says Eugene M. Johnson, Jr., chief scientific advisor at the Michael J. Fox Foundation. "You send us the grant, we'll review it on a rolling basis and get back to you within six weeks." The organization's founder, the Hollywood actor Michael J. Fox, began his eponymous foundation after he was diagnosed in his thirties with Parkinson's disease.

A Long Tradition of Philanthropically Funded Research

The Michael J. Fox Foundation is not the only biomedical philanthropy with ties to Hollywood. Created in 1953 by the famous industrialist and movie producer Howard Hughes, the Howard Hughes Medical Institute (HHMI) has been a driving force in the US biomedical research community for more than 50 years. "We believe in funding people not projects," says HHMI president Thomas Cech. "Our philosophy is to pick the best people and give them a lot of flexibility and autonomy," says Cech. The Institute spent $483 million on scientific research in 2005 and holds regular competitions to seek new investigators, who receive funding for 5 years. After those first 5 years, Hughes investigators are required to report back on what they've done, "So there is a day of reckoning, but there's a long period of quite dramatic freedom until then," say Cech. "We enable creativity by not being so hands on," says Cech. "The more constrained the funding of a project is, the more likely it will result in incremental increases in knowledge in an established field, which is not bad, but it's unlikely to completely change the way people think about science." Cech says HHMI will never become a substitute for the NIH but, rather, strives to compliment it. "The strong NIH in our country gives a nonprofit institute like us the opportunity and, we would say, the responsibility to not just add incrementally to governmental funding but to do something that cuts across the opportunities in a completely different direction," he says.

Across the Atlantic, Britain's Wellcome Trust, established in 1936 by Sir Henry Wellcome, also aims to support talented scientists so that they can undertake riskier research projects. "We make a difference by making brave grants to the very best people in the best places and not being risk averse," says Wellcome Trust director Mark Walport. "Good science is about asking important questions, and we fund the people who have important things to ask," says Walport. With a budget approximately twice that of HHMI, the Wellcome Trust is perhaps Europe's most influential biomedical funding agency and will spend approximately £540 million (US $1066 million) in 2007 to support 3500 researchers in 44 countries. Past projects the Trust has supported include everything from the human genome project to the development of the malaria drug artemisinin.

The Wellcome Trust provides roughly half of the UK's biomedical research funding and thus plays a crucial role in keeping the research enterprise going. Cech says that gives the Wellcome Trust a level of responsibility that the HHMI doesn't face. "If you're half of the total funding you can't say, ok, we're only going to fund bioengineers next year, because it would leave a lot of really strong work abandoned," he says. Even so, the Wellcome Trust does not try to substitute for public funding, and it specifically looks beyond the type of research that governments might support, says Walport. "We can ask diffi-

cult questions," he says. "We can act as an independent voice of reason in politically contentious areas," he says. For example, at the beginning of the HIV epidemic it wasn't clear how the disease was transmitted. "We funded a survey of young people's sexual habits—something the government at the time wasn't keen to do," says Walport.

But Europe is not depending solely on the largesse of the Wellcome Trust. Last March, philanthropy experts and researchers from throughout Europe gathered for a conference in Brussels entitled, "Giving More For Research in Europe: Strengthening the Role of Philanthropy in the Financing of Research." During the conference, Janez Potocnik, European commissioner for research, told attendees that, without question, philanthropic giving for research remains underdeveloped in most European countries. With the exception of the UK, most European nations do not have a strong culture of charitable giving for research, he said in a keynote speech. "We need to create an environment where giving is regarded positively by both donor and recipient." According to Potocnik, achieving this will require both a change in culture as well as tax credits and other government incentives for donors.

Money Can Come (and Go) Quickly

The ability to deliver money quickly is a hallmark of philanthropic groups. While red tape can make the process of procuring government funding a slow process, philanthropists can make speedy decisions, especially in the face of a pressing need. "We can move very, very quickly when we need to," says Richard Sprott, executive director of the Ellison Medical Foundation. As an example, he points to the anthrax scare in the US following the 9/11 attacks. Researchers wanted to find out what the background level of anthrax was in US post offices. "It would have taken the NIH years to find out. We called up an expert and had him funded in six weeks, and had an answer in six months."

"We fund many of the same people as the NIH does, but we can fund them for a new idea much more quickly than the NIH can," says Sprott. "It generally takes us less than six months from the grant application to the award." Still, such speed can also prove a minus, says Sprott. "We can just as easily take away the money. If we see a program isn't working we can end it." Indeed, in 2005, the Ellison Foundation halted its global infectious diseases program after deciding that they were not making enough of a difference in that field.

And then there's the insecurity inherent in taking funds from a single philanthropist. "We exist as long at Larry Ellison wants us to. He can pick up the phone and say it's over and it's over," says Sprott. Though Sprott says the Foundation looks safe at the moment, there's no guarantee. Ellison, the cofounder of the software corporation Oracle, was required to give $100 million to his foundation as part of a settlement with stockholders and recently cancelled a $115 million gift to Harvard University following the resignation of University president Larry Summers.

Many of today's donors are applying more scrutiny to their grantees than previous generations did, says Andrew Hastings, vice president of the National Philanthropic Trust in Jenkintown, Pennsylvania. "Donors are taking a more active role in their philanthropy, and expecting greater results. A generation ago, donors were more likely to support causes with unrestricted gifts. Now more donors are being more selective and specific with their grant-making." Lee-Ann Coleman, head of policy research at the Association of Medical Research Charities in London, has also seen this trend in the UK, and she says that many charities there are playing an active role in how research results are disseminated and applied. "The old fund and forget mentality is gone," says Mary Maxon, deputy vice chair of CIRM. "If they want something done, they're willing to pay for it, but they're not just going to give the money and walk away."

Some private organizations are moving to outcome-driven models. "The new funders don't just want to support research, they want to be partners in it," says Susan Fitzpatrick, vice president of the James S. McDonnell Foundation in Saint Louis, Missouri. Founded in 1950 by aerospace pioneer James S. McDonnell, the Foundation awarded $15.5 million worth of grants in 2004, much of it for research on neuroscience and brain cancer. Fitzpatrick says that today many foundations like hers are bringing patients, advocates, and clinicians into the decision-making process and they want to see tangible results. "This is not a basic science research institute. Some models that people study have no relevance to human disease and we're not going to fund those," says Fitzpatrick. "We gave three $2 million grants, which is a lot for a voluntary health organization, and we want a say in how the work gets done," says Fitzpatrick.

But success in raising research funds from philanthropic donors and foundations could come with a price. With philanthropic giving rising at an annual rate of six percent in the US, according to the National Philanthropic Trust, and a drive to bolster charitable giving in Europe, some worry that an influx of philanthropic money could lead governments to hand responsibility for biomedical research to the private sector. "You do worry about becoming an enabler and we hear anecdotally that that's happening," says Sprott. However, despite the start of the new Congress this month, US federal funding for R&D for FY2007 remains in limbo, and the NIH budget remains flat and may even fall. This situation provides a stark reminder that political tides and government budgets are constantly shifting, and that philanthropists will continue to play a key role in funding risky cutting-edge research for the foreseeable future.

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